

PNAS USA 93: 7381-7386 (1996); Narang et al., A displacement flow immunosensor for explosive detection using microcapillaries, *Anal. Chem.* 69:2779-2785 (1997); Shriver-Lake et al., *Biosens. Bioelect.* 12:1101-1106 (1997).

[0110] Carbohydrates may also be immobilized to a solid support, either to bind substances to the carbohydrate, or to immobilize another moiety (e.g., a protein) which is attached to the carbohydrate. See, e.g., U.S. Pat. No. 6,231,733, entitled "Immobilized Carbohydrate Biosensor", to Nilsson et al. The immobilized carbohydrate moiety may itself be specific for another type of biomolecule or structure, such as a protein, virus or a cell. A review of useful binding carbohydrate sequences can be found in, e.g., *Chemistry and Physics of Lipids*, vol. 42, p. 153-172, 1986, and in *Ann. Rev. Biochem.*, vol. 58, p. 309-350.

[0111] Methods for binding other biomolecules, as well as artificial molecules, substrates, ligands, and other molecules useful for binding biomolecules or biological substances of interest, depend on the nature of the substance to be bound and will be readily apparent to one of skill in the art. See, U.S. Pat. Nos. 5,817,470; 5,723,344; e.g., Weng et al., *Proteomics* 2:48-57 (2002); Zhou et al., *Trends Biotechnol* 10 (Suppl):S34-9 (2001); Mousses, et al., *Curr Opin Chem Biol* 6:97-101 (2002); Mirzabekov and Kolchinsky, *Curr Opin Chem Biol* 6:70-5 (2002); Reininger-Mack, *Trends Biotechnol* 20:56-61 (2002).

[0112] III. Probes and Target Molecules

[0113] The probes bound to the microarray substrate surface can be any type of molecule which binds or hybridizes with target molecules contained in the target liquid. The target molecules can be any type of molecule which binds or hybridizes with the immobilized probes. In various embodiments, a target molecule used in one assay can be immobilized on a substrate and used as a probe for another assay. Similarly, the probes used in one assay can be suspended in a fluid and used as a target molecule for another assay.

[0114] In accordance with various embodiments of the present invention, the probes can be, for example, deoxyribonucleic acids (DNA), ribonucleic acids (RNA), synthetic oligonucleotides, antibodies, proteins, peptides, lectins, modified polysaccharides, synthetic composite macromolecules, functionalized nanostructures, synthetic polymers, modified/blocked nucleotides/nucleosides, modified/blocked amino acids, fluorophores, chromophores, ligands, chelates, haptens and drug compounds. In some embodiments, the probes are polypeptides.

[0115] In particular embodiments, the biological target molecule is a polypeptide, a nucleic acid, a carbohydrate, a nucleoprotein, a glycopeptide or a glycolipid, preferably a polypeptide, which may be, for example, an enzyme, a hormone, a transcription factor, a receptor, a ligand for a receptor, a growth factor, an immunoglobulin, a steroid receptor, a nuclear protein, a signal transduction component, an allosteric enzyme regulator, and the like. The target molecule may comprise the chemically reactive group without prior modification of the target molecule or may be modified to comprise the chemically reactive group, for example, when a compound comprising the chemically reactive group is bound to the target molecule.

[0116] Other embodiments of the above described methods employ libraries of organic compounds which comprise

aldehydes, ketones, oximes, hydrazones, semicarbazones, carbazides, primary amines, secondary amines, tertiary amines, N-substituted hydrazines, hydrazides, alcohols, ethers, thiols, thioethers, thioesters, disulfides, carboxylic acids, esters, amides, ureas, carbamates, carbonates, ketals, thioketals, acetals, thioacetals, aryl halides, aryl sulfonates, alkyl halides, alkyl sulfonates, aromatic compounds, heterocyclic compounds, anilines, alkenes, alkynes, diols, amino alcohols, oxazolidines, oxazolines, thiazolidines, thiazolines, enamines, sulfonamides, epoxides, aziridines, isocyanates, sulfonyl chlorides, diazo compounds and/or acid chlorides, preferably aldehydes, ketones, primary amines, secondary amines, alcohols, thioesters, disulfides, carboxylic acids, acetals, anilines, diols, amino alcohols and/or epoxides, most preferably aldehydes, ketones, primary amines, secondary amines and/or disulfides.

[0117] Biological target molecules that find use in embodiments of the present invention include all biological molecules to which a small organic molecule may bind and preferably include, for example, polypeptides, nucleic acids, including both DNA and RNA, carbohydrates, nucleoproteins, glycoproteins, glycolipids, and the like. The biological target molecules that find use herein may be obtained in a variety of ways, including but not limited to commercially, synthetically, recombinantly, from purification from a natural source of the biological target molecule, etc.

[0118] In one embodiment, the biological target molecule is a polypeptide. Polypeptides that find use herein as targets for binding to organic molecule ligands include virtually any peptide or protein that comprises two or more amino acids and which possesses or is capable of being modified to possess a chemically reactive group for binding to a small organic molecule. Polypeptides of interest finding use herein may be obtained commercially, recombinantly, synthetically, by purification from a natural source, or otherwise and, for the most part are proteins, particularly proteins associated with a specific human disease condition, such as cell surface and soluble receptor proteins, such as lymphocyte cell surface receptors, enzymes, such as proteases and thymidylate synthetase, steroid receptors, nuclear proteins, allosteric enzyme inhibitors, clotting factors, serine/threonine kinases and dephosphorylases, threonine kinases and dephosphorylases, bacterial enzymes, fungal enzymes and viral enzymes, signal transduction molecules, transcription factors, proteins associated with DNA and/or RNA synthesis or degradation, immunoglobulins, hormones, receptors for various cytokines including, for example, erythropoietin/EPO, granulocyte colony stimulating receptor, granulocyte macrophage colony stimulating receptor thrombopoietin (TPO), IL-2, IL-3, IL-4, IL-5, IL-6, IL-10, IL-11, IL-12, growth hormone, prolactin, human placental lactogen (LPL), CNTF, octostatin, various chemokines and their receptors such as RANTES, (regulated upon activation, normal T cell expressed and secreted MIP1- α), IL-8, various ligands and receptors for tyrosine kinase such as insulin, insulin-like growth factor 1 (IGF-1), epidermal growth factor (EGF), heregulin- α and heregulin- β ., vascular endothelial growth factor (VEGF), placental growth factor (PLGF), tissue growth factors (TGF- α and TGF- β .), other hormones and receptors such as bone morphogenic factors, follicle stimulating hormone (FSH), and leutinizing hormone (LH), tissue necrosis factor (TNF),